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ULTRASHORT LASER PULSE EFFECTS ON OCULAR TISSUE: HISTOPATHOLOGIC ANALYSIS AND SURGICAL TECHNIQUES

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13. ABSTRACT *(Maximum 200 words)*

Toth et al. identified the acute pathologic retinal events which determined the extent of tissue damage from minimal laser energy and suprathreshold energy. She identified the acute pathology of primate maculas with minimal visible retinal lesions generated by 90 femtosscond and 5 picosecond pulses of 580 nm laser energy. Dr Toth's study included light microscopic evaluation of macular damage and electron microscopic ultrastructural analysis of melanosome ruptures within the retinal pigment epithelium. The pathology was reported at AFOSR with a CDROM summary of lesion data provided to armstrong Laboratory for reference. Dr Toth scored the area and extent of tissue damage and compiled a list for Dr Rockwell and Dr Clarence Cain at Armstrong Laboratory, Brooks, AFB for analysis and comparison to the ED50 MVL data. A paper summarizing this work has been published as the lead article in October, 1997 in Investigative Ophthalmology and Visual Science (IOVS). Dr Toth's Laboratory group gathered significant tissue data on ultrashort pulses of other laser wavelengths. They collaborated with Armstrong Laboratory (Dr Cain et al.) in analyzing near-infrared ultrashort laser pulse injury MVL data which was published at Society of Photo-Optical Instrumentation Engineers (SPIE), 1997 (Cair, Toth, et al.).

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Dr Toth also consulted with the Armstrong laboratory group on numerous related publications. She interpreted all macular fluorescein angiograms for the laser safety publications. Toth worked diligently at publishing the results of her research in the ophthalmic and engineering literature.

I. FINAL REPORT:

ULTRASHORT LASER PULSE EFFECTS ON OCULAR TISSUE: HISTOPATHOLOGIC ANALYSIS AND SURGICAL TECHNIQUES

Grant Number: F46920-95-1-0266

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15 April 1995 - 14 April 1998

II. OBJECTIVES:

Unchanged from Statement of Work

III. STATUS OF EFFORTS:

Toth et al. identified the acute pathologic retinal events which determined the extent of tissue damage from minimal laser energy and suprathreshold energy. She identified the acute pathology of primate maculas with minimal visible retinal lesions generated by 90 femtosecond and 5 picosecond pulses of 580 nm laser energy. Dr. Toth's study included light microsopic evaluation of macular damage and electron microscopic ultrastructural analysis of melanosome ruptures within the retinal pigment epithelium.

The pathology was reported to AFOSR with a CDROM summary of lesion data provided to Armstrong Laboratory for reference. Dr. Toth scored the area and extent of tissue damage and compiled a list for Dr. Rockwell and Dr. Clarence Cain at Armstrong Laboratory, Brooks, AFB for analysis and comparison to the ED50 MVL data. A paper summarizing this work has been published as the lead article in October, 1997 in *Investigative Ophthalmology and Visual Science* (IOVS).

Dr. Toth's Laboratory group gathered significant tissue data on ultrashort pulses of other laser wavelengths. They collaborated with Armstrong Laboratory (Dr. Cain et al.) in analyzing near-infrared ultrashort laser pulse injury MVL data which was published at *Society of Photo-Optical Instrumentation Engineers* (SPIE), 1997 (Cain, Toth, et al.).

Dr. Toth also consulted with the Armstrong laboratory group on numerous related publications. She interpreted all macular fluorescein angiograms for the laser safety publications. Toth worked diligently at publishing the results of her research in the ophthalmic and engineering literature.

IV. ACCOMPLISHMENTS / NEW FINDINGS:

Dr. Toth's histologic information regarding the effect of visible ultrashort laser pulses on the retina was reported to the military, scientific and medical laser and safety community. This new data included the first reports of the narrow columnar damage from ultrashort laser pulses, and supported the bench and theoretical work of Armstrong Laboratory. This histopathology report also demonstrated intraretinal, not choroidal, hemorrhages in relatively low energy lesions from fs and ps pulses. This validated our initial clinical observations and clarified theoretical predictions from the Armstrong Laboratory. With this histopathology, Toth demonstrated that the mechanism of injury is clearly quite different than that of longer pulsewidths. With the Armstrong group, Toth has shown that laser induced breakdown is a probable cause for lesions above threshold at 90 fs. Toth et al also demonstrated that ruptured melanosomes are not the cause of the MVL damage at 90 fs, though fractured and striated melanosomes are a component of higher energy suprathreshold lesions. This information was important to the interpretation of Dr. Glickman's studies of oxidative damage from ruptured melanosomes.

In collaboration with international scientists and the Armstrong laser group, Toth demonstrated the in vivo difference in evolution of a thermal laser lesion such as

from a cw argon laser versus evolution of a focal inner retinal lesion from an ultrashort laser pulse. Utilizing optical coherence tomography, she followed lesion evolution in vivo over the first seconds after laser delivery. In Archives of Ophthalmology, she published a report of this timecourse of development of edema, distortion of tissue and bleeding after laser delivery.

The histopathologic data was the first available for these ultrashort laser pulsewidths and has been essential to the military and civilian laser safety community as they determine safe standards for the use of ultrashort lasers. This data was previously requested by numerous military and civilian researchers, at national and international meetings and has been referenced at numerous laser meetings over the past several years. This data has also been of interest to the medical community as physicians considered the use of novel laser pulse structures for clinical applications in patient care. For the first time, clinicians knew which areas of the retina would be affected by low or high energy visible ultrashort laser pulses. As Toth demonstrated, focal retinal pigment epithelial damage can be created by these laser pulses without significantly affecting overlying neurosensory retina. Thus she proposed that ultrashort pulses might be a useful method for the future treatment of drusen associated with age-related macular degeneration.

The technical summary of the work is comprehensively covered in the publications listed below. These data will, therefore, not be repeated in this summary.

V. PERSONNEL SUPPORTED:

Personnel:	Job Title:
Cynthia A. Toth, M.D.	Principal Investigator
Diane Hatchell, Ph.D.	Co-Investigator
Alan D. Proia, M.D., Ph.D.	Pathologist
Ewa Worniallo	Histology Laboratory Analyst
Katrina Winter	Laboratory Research Analyst

Collaborators:

Dr. Benjamin A. Rockwell	Armstrong Laboratory, Brooks AFB, TX
Lt. Daniel X. Hammer	Armstrong Laboratory, Brooks AFB, TX
Maj. Cheryl D. DiCarlo	USUHS, Bethesda, MD
Capt. William P. Roach	AFOSR, Bolling AFB, DC
Dr. Clarence P. Cain	TASC, San Antonio, TX
Gary D. Noojin	TASC, San Antonio, TX
David J. Stolarski	TASC, San Antonio, TX

Other Academic Collaborators:

James G. Fujimoto, Ph.D.	Massachusetts Institute of Technology
Reginald Birngruber, Ph.D.	Medizinisches Laserzentrum Lubeck
Stephen A. Boppart, MSEE	Massachusetts Institute of Technology
Michael R. Hee Ph.D	Massachusetts Institute of Technology

VI. PUBLICATIONS:

Refereed Journals:

1. C.P. Cain, **C.A. Toth**, C.D. DiCarlo, C.D. Stein, G.D. Noojin, D.J. Stolarski, W.P. Roach. Visible retinal lesions from ultrashort laser pulses in the primate eye. Invest. Ophth. Vis. Sci. 36 (5): 879-888, 1995.

2. **C.A. Toth**, C.P. Cain, C.D. Stein, G.D. Noojin, D. Stolarski, J.A. Zuclich, W.P. Roach. Retinal effects of ultrashort laser pulses in the rabbit eye. Invest. Ophth. Vis. Sci. 36: 1910-1917, 1995.

3. C.P. Cain, C.D. DiCarlo, B.A. Rockwell, P.K. Kennedy, G.D. Noojin, D.J. Stolarski, D.X. Hammer, **C.A. Toth**, W.P. Roach. Retinal damage and laser-induced breakdown produced by ultrashort-pulses. Graefe's Arch. Clin. Ophth. (Suppl 1) 234: 28-37, 1996.

4. **C.A. Toth**, R. Birngruber, S.A. Boppart, M.R. Hee, J.G. Fujimoto, C.D. DiCarlo, E. A. Swanson, C.P. Cain, D.G. Narayan, G.D. Noojin, W.P. Roach. Argon laser retinal lesions evaluated *in vivo* by optical coherence tomography. Amer J of Ophth 123, (2) 188-198, 1997.

5. D.X. Hammer, G.D. Noojin, C.E. Clary, R.J. Thomas, **C.A. Toth**, B.A. Rockwell, W.P. Roach. Intraocular laser surgical probe (ILSP) for membrane ablation by laser-induced breakdown. Applied Optics, 36: (7): 1684-1693, 1997.

6. **C.A. Toth**, D.G. Narayan, C.P. Cain, G.D. Noojin, K.P. Winter, B.A. Rockwell, W.P. Roach. Pathology of macular lesions from subnanosecond pulses of visible laser energy. Invest. Ophthalmol & Vis Sci. 38: 11, 2204-2213, 1997.

7. **C.A. Toth**, D.G. Narayan, S.A. Boppart, M.R. Hee, J.G. Fujimoto, R. Birngruber, C.P. Cain, C.D. DiCarlo, W.P. Roach. A comparison of retinal morphology viewed by optical coherence tomography and by light microscopy. Archives of Ophthalmol. 115: 1425-1428, 1997.

8. W.P. Roach, **C.A. Toth**, D.G. Narayan, K.P. Winter, G.D. Noojin, C.D. DiCarlo, S.A. Boppart, M.R. Hee, R. Birngruber, J.G. Fujimoto, C.P. Cain. "The retinal response to picosecond laser pulses of varying energy and spot size." SUBMITTED, 1998.

Non-Refereed Journals:

1. **C.A. Toth**, D.X. Hammer, G.D. Noojin. Gradient-index lens multimode fiber probe for laser-induced optical breakdown in the eye. Society of Photo-Optical Instrumentation Engineers Proceedings, 2126: Ophthalmic Technologies IV. 291-304, 1994.

2. W.P. Roach, **C.A. Toth**, C.D. Stein, G.D. Noojin, D.J. Stolarski, C.P. Cain. Minimum visible retinal lesions from pico- and femtosecond laser pulses. SPIE Proceedings. 2134: 10-21, 1994.

3. C.P. Cain, **C.A. Toth**, C.D. Stein, G.D. Noojin, D.J. Stolarski, S.A. Boppart, W.P. Roach. Femtosecond laser thresholds: retinal damage versus induced breakdown mechanisms. SPIE Proceedings. 2134: 22-27, 1994.

4. C.D. Stein, **C.A. Toth**, C.P. Cain, G.D. Noojin, D.J. Stolarski, B.A. Rockwell, W.P. Roach. Retinal Hemorrhagic lesions from femtosecond visible pulses. SPIE Proceedings. 2134:28-36, 1994.

5. C.P. Cain, G.D. Noojin, D.J. Stolarski, **C.A. Toth**, C.D. DiCarlo, W.P. roach, C.D. Stein. Ultrashort pulse laser effects in the primate eye. USAF Technical Report AL/OE-TR-1994-0141 November 1994.

6. R. Birngruber, M.R. Hee, S.A. Boppart, J.G. Fujimoto, E.A. Swanson, **C.A. Toth**, C.D. DiCarlo, C.P. Cain, G.D. Noojin, W.P. Roach. *In-vivo* imaging of the development of linear and non-linear retinal laser effects using optical coherence tomography in correlation with histopathological finding. SPIE Proceedings, 2391:21-27 1995.

7. S.A. Boppart, M.R. Hee, J.G. Fujimoto, R. Birngruber, **C.A. Toth**, E.A. Swanson, C.P. Cain, G.D. Noojin, C.D. DiCarlo, W.P. Roach. Dynamic evolution and *in vivo* tomographic imaging of laser-induced retinal lesions using optical coherence tomography. Proceedings, Conference on Laser and Electro-Optics, 15: 417, 1995.

8. **C.A. Toth**, D.G. Narayan, C. Osborne, B.A. Rockwell, C.D. Stein, R.E. Amnote, C.D. DiCarlo, W.P. Roach, G.D. Noojin, C.P. Cain. Histopathology of ultrashort laser pulse retinal damage. SPIE Proceedings, 2681: 375-381, 1996.

9. B.A. Rockwell, D.X. Hammer, R.A. Hopkins, P.K. Payne, **C.A. Toth**, W.P. Roach, J.J. Druessel, P.K. Kennedy, R.E. Amnotte, B. Eilert, S. Phillips, G.D. Noojin, D.J. Stolarski and C.P. Cain. Ultrashort laser pulse bioeffects and safety. Proceedings of the International Laser Safety Conference 3: 159-165, 1997.

10. B.A. Rockwell, D.X. Hammer, R.A. Hopkins, D.J. Payne, **C.A. Toth**, D.G. Narayan, W.P. Roach, R. Birngruber, S.A. Boppart, M.R. Hee, C.D. DiCarlo, C.P. Cain, G.D. Noojin, J.G. Fujimoto. Optical coherence tomography of the retinal response to ultrashort laser pulses. SPIE Proceedings, 2975:126-132, 1997.

11. B.A. Rockwell, W.P. Roach, D.J. Payne, P.K. Kennedy, J.J. Druessel, R.E. Amnotte, B. Eilert, S. Phillips, D.J. Stolarski, G.D. Noojin, C P. Cain, **C.A. Toth**. Ultrashort laser pulse retinal damage, in laser and noncoherent ocular effects: epidemiology, prevention and treatment. SPIE Proceedings 2975: 60-65, 1997.

12. C.P. Cain, **C.A. Toth**, C.D. DiCarlo, G.D. Noojin, R.E. Amnotte, V. Caruthers, B.A. Rockwell. Visible lesion thresholds from near-infrared pico- and nanosecond laser pulses in the primate eye. Laser-Tissue Interaction VIII, SPIE Proceedings 2975:133-137, 1997.

13. **C.A. Toth**, D.G. Narayan, W.P. Roach, S.A. Boppart, M.R. Hee, J.G. Fujimoto, R. Birngruber, C.D. DiCarlo, C.P. Cain, G.D. Noojin. Analyzing retinal effects: old and new techniques. Conference on Lasers and Electro-Optics, 1997.

14. **C.A. Toth**, E.K. Chiu, J.M. Jumper, B.A. Rockwell. Damage mechanisms of pico- and femtosecond laser retinal lesions as viewed by electron microscopy. SPIE Proceedings, 3255: 77-81, 1998.

15. **C.A. Toth**, E.K. Chiu, K.P. Winter, C.P. Cain, G.D. Noojin, W.P. Roach. Windows of opportunity: applying ultrashort laser pulses for selective tissue effects. SPIE Proceedings, 3255: 122-125, 1998.

Published Abstracts:

1. C.D. Stein, **C.A. Toth**, C.P. Cain, D.J. Stolarski, G.D. Noojin, B.A. Rockwell, F.E. Cheney, L.N. McLin, W.P. Roach. Retinal effects of ultrashort laser pulses in Rhesus Monkeys. Invest. Ophth. Vis. Sci. 35(4): 1516, 1994.

2. **C.A. Toth**, D.X. Hammer, W.P. Roach. Gradient index (GRIN) optics for ophthalmic laser surgery. Invest. Ophth. Vis. Sci. 35(4): 1614, 1994.

3. C.D. Stein, **C.A. Toth**, C.P. Cain, G.D. Noojin, D.J. Stolarski, B.A. Rockwell, W.P. Roach. Retinal hemorrhagic lesions from femtosecond visible pulses. Laser-Tissue Interaction V. SPIE Proceedings 2134A: 10-21, 1994.

4. **C.A. Toth**, R. Birngruber, J.G. Fujimito, S.A. Boppart, M.R. Hee, C.D. DiCarlo, C.P. Cain, W.P. Roach. Correlation between optical coherence tomography, clinical examination and histopathology of macular laser lesions. Invest. Ophth. Vis. Sci. 36(4): 949, 1995.

5. R. Birngruber, M.R. Hee, S.A. Boppart, J.G. Fujimoto, E.A. Swanson, **C.A. Toth**, C.D. DiCarlo, C.P. Cain, G.D. Noojin, W.P. Roach. *In-vivo* imaging of the development of linear and non-linear retinal laser effects using optical coherence tomography in correlation with histopathological finding. SPIE Proceedings 2391: 1995

6. R. Birngruber, S.A. Boppart, **C.A. Toth**, M.R. Hee, J.G. Fujimoto, E.A. Swanson, C.D. DiCarlo, C.P. Cain G.D. Noojin, W.P. Roach. Optical coherence tomography of chorio-retinal structures: a new non-invasive diagnostic tool with microscopic resolution. Tagung der Deutschen Ophthalmologischen Gesellschaft 23-23.9 1995.

7. S.A. Boppart, MR. Hee, J.G. Fujimoto, R. Birngruber, **C.A. Toth**, E.A. Swanson, C.P. Cain, G.D. Noojin, C.D. DiCarlo, W.P. Roach. Dynamic evolution and *in vivo* tomographic Imaging of laser-induced optical coherence tomography. Conference on Lasers and Electro-Optics, 1995.

8. **C.A. Toth**, D.G. Narayan, C.P. Cain, C.D. DiCarlo, B.A. Rockwell, W.P. Roach. Histopathology of ultrashort pulse laser retinal laser retinal damage. Invest. Ophth. Vis. Sci. 37(3): 3170, 1996.

9. D.X. Hammer, G.D. Noojin, R.J. Thomas, C.E. Clary, B.A. Rockwell, **C.A. Toth**, W.P. Roach. Intraocular laser surgical probe for membrane disruption by laser-induced breakdown. Applied Optics, Vol. 36(7), March 1997.

10. A. Mansouri, **C.A. Toth**, K.P. Winter, C.P. Cain, G.D. Noojin, B.A. Rockwell. Retinal histopathology of suprathreshold ultrashort laser pulses. Invest Ophthal Vis Sci 38(4): 406, May 1997.

11. K.P. Winter, **C.A. Toth**, C.P. Cain, D.G. Narayan, C.D. DiCarlo, B.A. Rockwell, W.P. Roach. A damage mechanism for pico- and femtosecond visible laser retinal lesions. Invest Ophthal Vis Sci 38(4): 419, 1997.

12. **C.A. Toth**, D.G. Narayan, W.P. Roach, S.A. Boppart, M.R. Hee, J.G. Fujimoto, R. Birngruber, C.D. DiCarlo, C.P. Cain, G.D. Noojin. Analyzing retinal effects: old and new techniques. Conference on Lasers and Electro-Optics, 1997.

13. **C.A. Toth**, D.G. Narayan, K.P. Winter, W.P. Roach, C.P. Cain, G.D. Noojin, C.D. DiCarlo, S.A. Boppart, M.R. Hee, R. Birngruber, J.G. Fujimoto, B.A. Rockwell. Location of picosecond laser retinal injury varies with energy and spot size. Invest Ophthal Vis Sci 39(4): 481, 1998.

14. E.K. Chiu, J.M. Jumper, B.A. Rockwell, E. Worniallo, **C.A. Toth**. The response of the retinal pigment epithelium to pico- and femtosecond laser pulses as viewed by electron microscopy. Invest Ophthal Vis Sci 39(4): 482, 1998.

15. K.P. Winter, M.L. Norton, C.P. Cain, B.A. Rockwell, **C.A. Toth**. Single infrared ultrashort laser pulses may cause choroidal damage unless shielded by laser induced breakdown. Invest Ophthal Vis Sci 39(4): 4631, 1998.

16. **C.A. Toth**, E.K. Chiu, J.M. Jumper. The Ultrastructure of Picosecond and Femtosecond Pulse Laser Effects on the Retinal Pigment Epithelium, Bruch's Membrane and the Choroiocapillaris. SPIE, 1998.

VII. Transitions:

1997 Basic Research TechnologyTransitions: F46920-95-1-0226 Cynthia A. Toth, M.D., Duke University

Sub Area	Title	PM	Performer	Customer	Result	Application
X	Ultrashort laser bioeffects	Kozumbo	Cynthia A. Toth, M.D. Duke University Eye Center (919) 684-5631	Dr Benjamin A. Rockwell AL/OEDL, Brooks AFB, TX (210)536-4790	Transmission electron micrographs of ultrashort effects on the RPE demonstrate striate and fractured melanosomes	Data supported the concept of microbubble effects as well as LIB.
X	Ultrashort laser bioeffects	Kozumbo	Cynthia A. Toth, M.D. Duke University Eye Center (919) 684-5631	Dr. Dave Sliney, (410)671-3932, Am. Conf. of Govt & Industrial Hygienists (ACGIH)	Comprehensive histopathology documenting the minimal level of pathologic response to ultrashort laser pulses in IOVS publication	Comprehensive data to be used in establishing national laser safety standards, i.e., the maximum permissible exposure (MPE) limits of ultrashort laser pulses
X	Ultrashort laser bioeffects	Kozumbo	Cynthia A. Toth, M.D. Duke University Eye Center (919) 684-5631	Dr Benjamin Rockwell, AL/OEDL, Brooks AFB, TX (210)536-4790	Histopathology data demonstratingchoroidal damage from the first infrared laser retinal injuries	Data demonstrate a different retinal effect at short pulsewidths with wavelength dependence
X	Ultrashort laser bioeffects	Kozumbo	Cynthia A. Toth, M.D. Duke University Eye Center (919) 684-5631	Dr. Charles Lin Wellman Labs 617-724-3957	Light micrographs of ultrashort primate lesions show lifting and vacuolization which supports his microbubble theory	Photomicrographs provided information to assisted in understanding the clinical effects of microbubble theory
X	Ultrashort laser bioeffects	Kozumbo	Cynthia A. Toth, M.D. Duke University Eye Center (919) 684-5631	Dr. Charles Lin Wellman Labs 617-724-3957	Melanosome response to femtosecond laser pulses includes ruptured and striated melanosomes in moderate lesions	Data assisted in his evaluation of aqueous versus melanosome based plasma formation versus bubble formation
X	Ultrashort laser bioeffects	Kozumbo	Cynthia A. Toth, M.D. Duke University Eye Center (919) 684-5631	Dr. Clarence P.Cain The Analytic ScienceCorp San Antonio, TX (210) 536-4794	Fluorescein angiography data on laser lesions of primate retina	Data changed the previously held concept that fluorescein angiograms are more sensitive for the identification of retinal injury and support novel theories of laser effects
X	Ultrashort laser bioeffects	Kozumbo	Cynthia A. Toth, M.D. Duke University Eye Center (919) 684-5631	Bobbie Geunther, PhD Duke FEL facility 919-660-2674	Overview of pulsed laser effects on ocular tissue	Demonstrated potential benefits of careful histopathology in the FEL studies
X	Ultrashort laser bioeffects	Kozumbo	Cynthia A. Toth, M.D. Duke University Eye Center (919) 684-5631	Dr.Steve Jacques UT Health Science Center	Melanosome response to femtosecond laser pulses: striated melanosomes are also present in moderate lesions	Melanosome data utilized for theoretical calculations of stress confinement effects from femtosecond laser pulses
X	Ultrashort laser bioeffects	Kozumbo	Cynthia A. Toth, M.D. Duke University Eye Center (919) 684-5631	Dr. Randy Glickman UT Health Science Center	Melanosome response to femtosecond laser pulses: striated melanosomes are also present in moderate lesions	Melanosome data may further modify the theory of superoxide injury from melanosome ruture at threshold
X	Ultrashort laser bioeffects	Kozumbo	Cynthia A. Toth, M.D. Duke University Eye Center (919) 684-5631	VayTek, Fairfield Iowa 515-472-2227	Three dimensional imaging software applied to transmission electron micrographs	Transferred to industry a novel method of imaging ultrastructure of the retinal pigment epithelium
X	Ultrashort laser bioeffects	Kozumbo	Cynthia A. Toth, M.D. Duke University Eye Center (919) 684-5631	ANSI subcommittee for laser safety standards update William P.Roach	Laser injury data for ultrashort laser pulses to the eye with interpretation of effect on risk of injury with vision loss	Transferred information essential to the decision regarding modification of the national safety guidelines below 1 ns laser pulse
X	Ultrashort laser bioeffects	Kozumbo	Cynthia A. Toth, M.D. Duke University Eye Center (919) 684-5631	International Ophthalmic community	Clinicopathologic correlation of laser retinal lesions and optical coherence tomography	Demonstrated a novel method of analysis of ocular tissue response to laser injury in a publication
X	Ultrashort laser bioeffects	Kozumbo	Cynthia A. Toth, M.D. Duke University Eye Center (919) 684-5631	Infinitech 69 Highlands Way Oxford, GA(770)385-5470	Patented intraocular laser surgical probe for ocular incisions	Infinitech expressed interest in the newly patented technology.
X	Ultrashort laser bioeffects	Kozumbo	Cynthia A. Toth, M.D. Duke University Eye Center (919) 684-5631	Humphrey Instruments San Leandro CA Jay Wei (510) 895-9110	Information regarding applications of optical coherence tomography of evolving laser and retinal lesions.	Meetings with Humphrey OCT development team to explain utilization of OCT technology for laser imaging. Advised Humphrey regarding optimizing the system for useful retinal data.

VIII. NEW DISCOVERIES, INVENTIONS, OR PATENT DISCLOSURES:

- Our published comprehensive studies provide much basic data, for the ANSI "Standard for the safe use of lasers" revision to include ultrashort laser pulses. This data will thus also be used for military laser standards. This data will similarly be used by the European community when the "IEC International Standard for the Safety of Laser Products" is revised to include ultrashort laser pulses.

- U.S. Patent (08/367,602) Issued April, 1998, on Intraocular Laser Surgical Probe (ILSP) for membrane ablation by laser-induced breakdown. Hammer, Toth, Roach.